# 10/570011 IAP9 Rec'd PCT/PTO 01 MAR 2006

205

253

# 0701012W01.ST25.txt SEQUENCE LISTING

| <110> | Kureha  | Chemical               | Industry | Company, | Limited |
|-------|---------|------------------------|----------|----------|---------|
|       | KAMATA, | Toru                   |          |          |         |
|       | MITSUSH | [TA, Junj <sup>.</sup> | i        |          |         |
|       |         |                        |          |          |         |

<120> Antibodies to Nox1 polypeptide, method for the detection of cancer using Nox1 gene and method for screening substances suppressing cancer growth

| NOXI gene and method for screening substances suppressing cancer grow  |     |
|--|-----|
| <130> 0701012w01   |     |
| <160> 27   |     |
| <170> PatentIn version 3.1   |     |
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| <211> 1734   |     |
| <212> DNA  |     |
| <213> Homo sapiens   |     |
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| <221> CDS  |     |
| <222> (71)(1618)   |     |
| <223> Human Nox1 polypeptide of SEQ NO:2   |     |
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| cctcttgaca atg gga aac tgg gtg gtt aac cac tgg ttt tca gtt ttg<br>Met Gly Asn Trp Val Val Asn His Trp Phe Ser Val Leu<br>1 5 10                | 109 |
| ttt ctg gtt gtt tgg tta ggg ctg aat gtt ttc ctg ttt gtg gat gcc<br>Phe Leu Val Val Trp Leu Gly Leu Asn Val Phe Leu Phe Val Asp Ala<br>15 20 25 | 157 |

ctt ggg tca aca ttg gcc tgt gcc cga gcg tct gct ctc tgc ttg aat Leu Gly Ser Thr Leu Ala Cys Ala Arg Ala Ser Ala Leu Cys Leu Asn 50 55 60 Page 1

ttc ctg aaa tat gag aag gcc gac aaa tac tac tac aca aga aaa atc Phe Leu Lys Tyr Glu Lys Ala Asp Lys Tyr Tyr Tyr Thr Arg Lys Ile 30 40 45

| ttt<br>Phe        | aac<br>Asn        | agc<br>Ser        | acg<br>Thr<br>65  | ctg<br>Leu        | atc<br>Ile        | ctg<br>Leu        | ctt<br>Leu        | cct<br>Pro<br>70  | gtg<br>Val        | tgt<br>Cys          | cgc<br>Arg        | aat<br>Asn        | ctg<br>Leu<br>75  | ctg<br>Leu        | tcc<br>Ser        | 301  |
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| ttg<br>Leu        | gat<br>Asp<br>95  | cac<br>His        | aac<br>Asn        | ctc<br>Leu        | acc<br>Thr        | ttc<br>Phe<br>100 | cac<br>His        | aag<br>Lys        | ctg<br>Leu        | gtg<br>Val          | gcc<br>Ala<br>105 | tat<br>Tyr        | atg<br>Met        | atc<br>Ile        | tgc<br>Cys        | 397  |
| cta<br>Leu<br>110 | cat<br>His        | aca<br>Thr        | gct<br>Ala        | att<br>Ile        | cac<br>His<br>115 | atc<br>Ile        | att<br>Ile        | gca<br>Ala        | cac<br>His        | ctg<br>Leu<br>120   | ttt<br>Phe        | aac<br>Asn        | ttt<br>Phe        | gac<br>Asp        | tgc<br>Cys<br>125 | 445  |
| tat<br>Tyr        | agc<br>Ser        | aga<br>Arg        | agc<br>Ser        | cga<br>Arg<br>130 | cag<br>Gln        | gcc<br>Ala        | aca<br>Thr        | gat<br>Asp        | ggc<br>Gly<br>135 | tcc<br>Ser          | ctt<br>Leu        | gcc<br>Ala        | tcc<br>Ser        | att<br>Ile<br>140 | ctc<br>Leu        | 493  |
| tcc<br>Ser        | agc<br>Ser        | cta<br>Leu        | tct<br>Ser<br>145 | cat<br>His        | gat<br>Asp        | gag<br>Glu        | aaa<br>Lys        | aag<br>Lys<br>150 | ggg<br>Gly        | ggt<br>Gly          | tct<br>Ser        | tgg<br>Trp        | cta<br>Leu<br>155 | aat<br>Asn        | ccc<br>Pro        | 541  |
| atc<br>Ile        | cag<br>Gln        | tcc<br>Ser<br>160 | cga<br>Arg        | aac<br>Asn        | acg<br>Thr        | aca<br>Thr        | gtg<br>Val<br>165 | gag<br>Glu        | tat<br>Tyr        | gtg<br>Val          | aca<br>Thr        | ttc<br>Phe<br>170 | acc<br>Thr        | agc<br>Ser        | att<br>Ile        | 589  |
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| act<br>Thr<br>190 | tca<br>Ser        | gct<br>Ala        | act<br>Thr        | gag<br>Glu        | ttc<br>Phe<br>195 | atc<br>Ile        | cgg<br>Arg        | agg<br>Arg        | agt<br>Ser        | tat<br>Tyr<br>200   | ttt<br>Phe        | gaa<br>Glu        | gtc<br>val        | ttc<br>Phe        | tgg<br>Trp<br>205 | 685  |
| tat<br>Tyr        | act<br>Thr        | cac<br>His        | cac<br>His        | ctt<br>Leu<br>210 | ttt<br>Phe        | atc<br>Ile        | ttc<br>Phe        | tat<br>Tyr        | atc<br>Ile<br>215 | ctt<br>Leu          | ggc<br>Gly        | tta<br>Leu        | ggg<br>Gly        | att<br>Ile<br>220 | cac<br>His        | 733  |
| ggc<br>Gly        | att<br>Ile        | ggt<br>Gly        | gga<br>Gly<br>225 | att<br>Ile        | gtc<br>Val        | cgg<br>Arg        | ggt<br>Gly        | caa<br>Gln<br>230 | aca<br>Thr        | gag<br>Glu          | gag<br>Glu        | agc<br>Ser        | atg<br>Met<br>235 | aat<br>Asn        | gag<br>Glu        | 781  |
| agt<br>Ser        | cat<br>His        | cct<br>Pro<br>240 | cgc<br>Arg        | aag<br>Lys        | tgt<br>Cys        | Ala               | gag<br>Glu<br>245 | tct<br>Ser        | ttt<br>Phe        | gag<br>Glu          | atg<br>Met        | tgg<br>Trp<br>250 | gat<br>Asp        | gat<br>Asp        | cgt<br>Arg        | 829  |
| gac<br>Asp        | tcc<br>Ser<br>255 | cac<br>His        | tgt<br>Cys        | agg<br>Arg        | cgc<br>Arg        | cct<br>Pro<br>260 | aag<br>Lys        | ttt<br>Phe        | gaa<br>Glu        | ggg<br>Gly          | cat<br>His<br>265 | ccc<br>Pro        | cct<br>Pro        | gag<br>Glu        | tct<br>Ser        | 877  |
| tgg<br>Trp<br>270 | aag<br>Lys        | tgg<br>Trp        | atc<br>Ile        | ctt<br>Leu        | gca<br>Ala<br>275 | ccg<br>Pro        | gtc<br>Val        | att<br>Ile        | ctt<br>Leu        | tat<br>Tyr<br>280   | atc<br>Ile        | tgt<br>Cys        | gaa<br>Glu        | agg<br>Arg        | atc<br>Ile<br>285 | 925  |
| ctc<br>Leu        | cgg<br>Arg        | ttt<br>Phe        | tac<br>Tyr        | cgc<br>Arg<br>290 | tcc<br>Ser        | cag<br>Gln        | cag<br>Gln        | aag<br>Lys        | gtt<br>Val<br>295 | gtg<br>Val          | att<br>Ile        | acc<br>Thr        | aag<br>Lys        | gtt<br>Val<br>300 | gtt<br>Val        | 973  |
| atg<br>Met        | cac<br>His        | cca<br>Pro        | tcc<br>Ser<br>305 | aaa<br>Lys        | gtt<br>Val        | ttg<br>Leu        | gaa<br>Glu        | ttg<br>Leu<br>310 | cag<br>Gln        | atg<br>Met          | aac<br>Asn        | aag<br>Lys        | cgt<br>Arg<br>315 | ggc<br>Gly        | ttc<br>Phe        | 1021 |
| agc<br>Ser        | atg<br>Met        | gaa<br>Glu        | gtg<br>Val        | ggg<br>Gly        | cag<br>Gln        | tat<br>Tyr        | atc<br>Ile        | ttt<br>Phe        | Val               | aat<br>Asn<br>age 2 | Cys               | ccc<br>Pro        | tca<br>Ser        | atc<br>Ile        | tct<br>Ser        | 1069 |

|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 330               |                   |                   |                   |      |
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| ttc<br>Phe<br>350 | ttc<br>Phe        | tcc<br>Ser        | att<br>Ile        | cat<br>His        | atc<br>Ile<br>355 | cga<br>Arg        | gca<br>Ala        | gca<br>Ala        | ggg<br>Gly        | gac<br>Asp<br>360 | tgg<br>Trp        | aca<br>Thr        | gaa<br>Glu        | aat<br>Asn        | ctc<br>Leu<br>365 | 1165 |
| ata<br>Ile        | agg<br>Arg        | gct<br>Ala        | ttc<br>Phe        | gaa<br>Glu<br>370 | caa<br>Gln        | caa<br>Gln        | tat<br>Tyr        | tca<br>Ser        | cca<br>Pro<br>375 | att<br>Ile        | ccc<br>Pro        | agg<br>Arg        | att<br>Ile        | gaa<br>Glu<br>380 | gtg<br>Val        | 1213 |
| gat<br>Asp        | ggt<br>Gly        | ccc<br>Pro        | ttt<br>Phe<br>385 | ggc<br>Gly        | aca<br>Thr        | gcc<br>Ala        | agt<br>Ser        | gag<br>G1u<br>390 | gat<br>Asp        | gtt<br>Val        | ttc<br>Phe        | cag<br>Gln        | tat<br>Tyr<br>395 | gaa<br>Glu        | gtg<br>val        | 1261 |
| gct<br>Ala        | gtg<br>Val        | ctg<br>Leu<br>400 | gtt<br>Val        | gga<br>Gly        | gca<br>Ala        | gga<br>Gly        | att<br>Ile<br>405 | ggg<br>Gly        | gtc<br>Val        | acc<br>Thr        | ccc<br>Pro        | ttt<br>Phe<br>410 | gct<br>Ala        | tct<br>Ser        | atc<br>Ile        | 1309 |
| ttg<br>Leu        | aaa<br>Lys<br>415 | tcc<br>Ser        | atc<br>Ile        | tgg<br>Trp        | tac<br>Tyr        | aaa<br>Lys<br>420 | ttc<br>Phe        | cag<br>Gln        | tgt<br>Cys        | gca<br>Ala        | gac<br>Asp<br>425 | cac<br>His        | aac<br>Asn        | ctc<br>Leu        | aaa<br>Lys        | 1357 |
| aca<br>Thr<br>430 | aaa<br>Lys        | aag<br>Lys        | gtt<br>Val        | ggt<br>Gly        | cat<br>His<br>435 | gca<br>Ala        | gca<br>Ala        | tta<br>Leu        | aac<br>Asn        | ttt<br>Phe<br>440 | gac<br>Asp        | aag<br>Lys        | gcc<br>Ala        | act<br>Thr        | gac<br>Asp<br>445 | 1405 |
| atc<br>Ile        | gtg<br>Val        | aca<br>Thr        | ggt<br>Gly        | ctg<br>Leu<br>450 | aaa<br>Lys        | cag<br>Gln        | aaa<br>Lys        | acc<br>Thr        | tcc<br>Ser<br>455 | ttt<br>Phe        | ggg<br>Gly        | aga<br>Arg        | cca<br>Pro        | atg<br>Met<br>460 | tgg<br>Trp        | 1453 |
| gac<br>Asp        | aat<br>Asn        | gag<br>Glu        | ttt<br>Phe<br>465 | tct<br>Ser        | aca<br>Thr        | ata<br>Ile        | gct<br>Ala        | acc<br>Thr<br>470 | tcc<br>Ser        | cac<br>His        | ccc<br>Pro        | aag<br>Lys        | tct<br>Ser<br>475 | gta<br>Val        | gtg<br>Val        | 1501 |
| gga<br>Gly        | gtt<br>Val        | ttc<br>Phe<br>480 | tta<br>Leu        | tgt<br>Cys        | ggc<br>Gly        | cct<br>Pro        | cgg<br>Arg<br>485 | act<br>Thr        | ttg<br>Leu        | gca<br>Ala        | aag<br>Lys        | agc<br>Ser<br>490 | ctg<br>Leu        | cgc<br>Arg        | aaa<br>Lys        | 1549 |
| tgc<br>Cys        | tgt<br>Cys<br>495 | cac<br>His        | cga<br>Arg        | tat<br>Tyr        | tcc<br>Ser        | agt<br>Ser<br>500 | ctg<br>Leu        | gat<br>Asp        | cct<br>Pro        | aga<br>Arg        | aag<br>Lys<br>505 | gtt<br>Val        | caa<br>Gln        | ttc<br>Phe        | tac<br>Tyr        | 1597 |
| ttc<br>Phe<br>510 | aac<br>Asn        | aaa<br>Lys        | gaa<br>Glu        | aat<br>Asn        | ttt<br>Phe<br>515 | tga               | gtta              | ıtagg             | aa t              | aagg              | acgg              | jt aa             | ıtctg             | catt              | :                 | 1648 |
| ttgt              | ctct              | tt g              | tato              | ttca              | ıg ta             | attt              | actt              | ggt               | ctcg              | tca               | ggtt              | tgag              | jca g             | tcac              | tttag             | 1708 |
| gata              | agaa              | itg t             | gcct              | ctca              | a go              | cttg              | )                 |                   |                   |                   |                   |                   |                   |                   |                   | 1734 |
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<211> 515

<212> PRT

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0701012W01.ST25.txt

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Ile Leu Ala Pro Val Ile Leu Tyr Ile Cys Glu Arg Ile Leu Arg Phe 275 280 285

Tyr Arg Ser Gln Gln Lys Val Val Ile Thr Lys Val Val Met His Pro 290 295 300

Ser Lys Val Leu Glu Leu Gln Met Asn Lys Arg Gly Phe Ser Met Glu 305 310 315 320

Val Gly Gln Tyr Ile Phe Val Asn Cys Pro Ser Ile Ser Leu Leu Glu 325 330 335

Trp His Pro Phe Thr Leu Thr Ser Ala Pro Glu Glu Asp Phe Phe Ser 340 345 350

Ile His Ile Arg Ala Ala Gly Asp Trp Thr Glu Asn Leu Ile Arg Ala 355 360 365

Phe Glu Gln Gln Tyr Ser Pro Ile Pro Arg Ile Glu Val Asp Gly Pro 370 380

Phe Gly Thr Ala Ser Glu Asp Val Phe Gln Tyr Glu Val Ala Val Leu 385 390 395 400

Val Gly Ala Gly Ile Gly Val Thr Pro Phe Ala Ser Ile Leu Lys Ser 405 410 415

Ile Trp Tyr Lys Phe Gln Cys Ala Asp His Asn Leu Lys Thr Lys Lys 420 425 430

Val Gly His Ala Ala Leu Asn Phe Asp Lys Ala Thr Asp Ile Val Thr 435 440 445

Gly Leu Lys Gln Lys Thr Ser Phe Gly Arg Pro Met Trp Asp Asn Glu 450 460

Phe Ser Thr Ile Ala Thr Ser His Pro Lys Ser Val Val Gly Val Phe 465 470 475 480

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| <213             | > F               | Rattu             | is no             | rveg              | jicus             | ;                 |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
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| <223             | '> F              | Rat N             | lox1              | poly              | /pept             | ide               | of s              | SEQ N             | 10:4              |                   |                   |                   |                   |                   |                   |     |
| <400<br>ttct     |                   | •                 | gtgtg             | catt              | t ga              | ıgtgt             | cata              | a aag             | jacat             | ata               | tctt              | gago              | cta g             | gacag             | gaagtt            | 60  |
|                  |                   |                   |                   |                   |                   |                   |                   | _                 | _                 |                   |                   |                   |                   | _                 | ctcca             | 120 |
| tttg             | aca               | atg<br>Met<br>1   | gga<br>Gly        | aac<br>Asn        | tgg<br>Trp        | ctg<br>Leu<br>5   | gtt<br>Val        | aac<br>Asn        | cac<br>His        | tgg<br>Trp        | ctc<br>Leu<br>10  | tca<br>Ser        | gtt<br>Val        | ttg<br>Leu        | ttt<br>Phe        | 169 |
| ctg<br>Leu<br>15 | gtt<br>Val        | tct<br>Ser        | tgg<br>Trp        | ttg<br>Leu        | ggg<br>G1y<br>20  | ctg<br>Leu        | aac<br>Asn        | att<br>Ile        | ttt<br>Phe        | ctg<br>Leu<br>25  | ttt<br>Phe        | gtg<br>Val        | tac<br>Tyr        | gtc<br>val        | ttc<br>Phe<br>30  | 217 |
| ctg<br>Leu       | aat<br>Asn        | tat<br>Tyr        | gag<br>Glu        | aag<br>Lys<br>35  | tct<br>Ser        | gac<br>Asp        | aag<br>Lys        | tac<br>Tyr        | tat<br>Tyr<br>40  | tac<br>Tyr        | acg<br>Thr        | aga<br>Arg        | gaa<br>Glu        | att<br>Ile<br>45  | ctc<br>Leu        | 265 |
| gga<br>Gly       | act<br>Thr        | gcc<br>Ala        | ttg<br>Leu<br>50  | gcc<br>Ala        | ttg<br>Leu        | gcc<br>Ala        | aga<br>Arg        | gca<br>Ala<br>55  | tct<br>Ser        | gct<br>Ala        | ttg<br>Leu        | tgc<br>Cys        | ctg<br>Leu<br>60  | aat<br>Asn        | ttt<br>Phe        | 313 |
| aac<br>Asn       | agc<br>Ser        | atg<br>Met<br>65  | gtg<br>Val        | atc<br>Ile        | ctg<br>Leu        | att<br>Ile        | cct<br>Pro<br>70  | gtg<br>Val        | tgt<br>Cys        | cga<br>Arg        | aat<br>Asn        | ctg<br>Leu<br>75  | ctc<br>Leu        | tcc<br>Ser        | ttc<br>Phe        | 361 |
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| gat<br>Asp<br>95 | cac<br>His        | aac<br>Asn        | ctc<br>Leu        | acc<br>Thr        | ttc<br>Phe<br>100 | cat<br>His        | aag<br>Lys        | ctg<br>Leu        | gtg<br>Val        | gca<br>Ala<br>105 | tat<br>Tyr        | atg<br>Met        | atc<br>Ile        | tgc<br>Cys        | ata<br>Ile<br>110 | 457 |
| ttc<br>Phe       | aca<br>Thr        | gct<br>Ala        | att<br>Ile        | cat<br>His<br>115 | atc<br>Ile        | att<br>Ile        | gca<br>Ala        | cat<br>His        | cta<br>Leu<br>120 | ttt<br>Phe        | aac<br>Asn        | ttt<br>Phe        | gaa<br>Glu        | cgc<br>Arg<br>125 | tac<br>Tyr        | 50! |
| agt<br>Ser       | aga<br>Arg        | agc<br>Ser        | caa<br>Gln<br>130 | cag<br>Gln        | gcc<br>Ala        | atg<br>Met        | gat<br>Asp        | gga<br>Gly<br>135 | tct<br>Ser        | ctt<br>Leu        | gcc<br>Ala        | tct<br>Ser        | gtt<br>Val<br>140 | ctc<br>Leu        | tcc<br>Ser        | 553 |
| agc<br>Ser       | cta<br>Leu        | ttc<br>Phe<br>145 | cat<br>His        | ccc<br>Pro        | gag<br>Glu        | aaa<br>Lys        | gaa<br>Glu<br>150 | gat<br>Asp        | tct<br>Ser        | tgg<br>Trp        | cta<br>Leu        | aat<br>Asn<br>155 | ccc<br>Pro        | atc<br>Ile        | cag<br>Gln        | 60: |
| tct<br>Ser       | cca<br>Pro<br>160 | aac<br>Asn        | gtg<br>Val        | aca<br>Thr        | gtg<br>Val        | atg<br>Met<br>165 | tat<br>Tyr        | gca<br>Ala        | gca<br>Ala        | ttt<br>Phe        | acc<br>Thr<br>170 | agt<br>Ser        | att<br>Ile        | gct<br>Ala        | ggc<br>Gly        | 649 |

| c++               | act               | 003               | ata               | atc               | 200               | ac+               |                   | 0701              |                   |                   |                   |                   | a+3               | 26+               | +62               | 607  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| Leu<br>175        | Thr               | Gly               | val               | val               | Ala<br>180        | Thr               | val               | gct<br>Ala        | Leu               | val<br>185        | Leu               | Met               | Val               | Thr               | Ser<br>190        | 697  |
| gct<br>Ala        | atg<br>Met        | gag<br>Glu        | ttt<br>Phe        | atc<br>Ile<br>195 | cgc<br>Arg        | agg<br>Arg        | aat<br>Asn        | tat<br>Tyr        | ttt<br>Phe<br>200 | gag<br>Glu        | ctc<br>Leu        | ttc<br>Phe        | tgg<br>Trp        | tat<br>Tyr<br>205 | aca<br>Thr        | 745  |
| cat<br>His        | cac<br>His        | ctt<br>Leu        | ttc<br>Phe<br>210 | atc<br>Ile        | atc<br>Ile        | tat<br>Tyr        | atc<br>Ile        | atc<br>Ile<br>215 | tgc<br>Cys        | tta<br>Leu        | ggg<br>Gly        | atc<br>Ile        | cat<br>His<br>220 | ggc<br>Gly        | ctg<br>Leu        | 793  |
| ggg<br>Gly        | ggg<br>Gly        | att<br>Ile<br>225 | gtc<br>Val        | cgg<br>Arg        | ggt<br>Gly        | caa<br>Gln        | aca<br>Thr<br>230 | gaa<br>Glu        | gag<br>Glu        | agc<br>Ser        | atg<br>Met        | agt<br>Ser<br>235 | gaa<br>Glu        | agt<br>Ser        | cat<br>His        | 841  |
| ccc<br>Pro        | cgc<br>Arg<br>240 | aac<br>Asn        | tgt<br>Cys        | tca<br>Ser        | tac<br>Tyr        | tct<br>Ser<br>245 | ttc<br>Phe        | cac<br>His        | gag<br>Glu        | tgg<br>Trp        | gat<br>Asp<br>250 | aag<br>Lys        | tat<br>Tyr        | gaa<br>Glu        | agg<br>Arg        | 889  |
| agt<br>Ser<br>255 | tgc<br>Cys        | agg<br>Arg        | agt<br>Ser        | cct<br>Pro        | cat<br>His<br>260 | ttt<br>Phe        | gtg<br>Val        | ggg<br>Gly        | caa<br>Gln        | ccc<br>Pro<br>265 | cct<br>Pro        | gag<br>Glu        | tct<br>Ser        | tgg<br>Trp        | aag<br>Lys<br>270 | 937  |
| tgg<br>Trp        | atc<br>Ile        | ctc<br>Leu        | gcg<br>Ala        | ccg<br>Pro<br>275 | att<br>Ile        | gct<br>Ala        | ttt<br>Phe        | tat<br>Tyr        | atc<br>Ile<br>280 | ttt<br>Phe        | gaa<br>Glu        | agg<br>Arg        | atc<br>Ile        | ctt<br>Leu<br>285 | cgc<br>Arg        | 985  |
| ttt<br>Phe        | tat<br>Tyr        | cgc<br>Arg        | tcc<br>Ser<br>290 | cgg<br>Arg        | cag<br>Gln        | aag<br>Lys        | gtc<br>Val        | gtg<br>Val<br>295 | att<br>Ile        | acc<br>Thr        | aag<br>Lys        | gtt<br>Val        | gtc<br>Val<br>300 | atg<br>Met        | cac<br>His        | 1033 |
| cca<br>Pro        | tgt<br>Cys        | aaa<br>Lys<br>305 | gtt<br>val        | ttg<br>Leu        | gaa<br>Glu        | ttg<br>Leu        | cag<br>Gln<br>310 | atg<br>Met        | agg<br>Arg        | aag<br>Lys        | cgg<br>Arg        | ggc<br>Gly<br>315 | ttt<br>Phe        | act<br>Thr        | atg<br>Met        | 1081 |
| gga<br>Gly        | ata<br>Ile<br>320 | gga<br>Gly        | cag<br>Gln        | tat<br>Tyr        | ata<br>Ile        | ttc<br>Phe<br>325 | gta<br>Val        | aat<br>Asn        | tgc<br>Cys        | ccc<br>Pro        | tcg<br>Ser<br>330 | att<br>Ile        | tcc<br>Ser        | ttc<br>Phe        | ctg<br>Leu        | 1129 |
| gaa<br>Glu<br>335 | tgg<br>Trp        | cat<br>His        | ccc<br>Pro        | ttt<br>Phe        | act<br>Thr<br>340 | ctg<br>Leu        | acc<br>Thr        | tct<br>Ser        | gct<br>Ala        | cca<br>Pro<br>345 | gag<br>Glu        | gaa<br>Glu        | gaa<br>Glu        | ttt<br>Phe        | ttc<br>Phe<br>350 | 1177 |
| tcc<br>Ser        | att<br>Ile        | cat<br>His        | att<br>Ile        | cga<br>Arg<br>355 | gca<br>Ala        | gca<br>Ala        | ggg<br>Gly        | gac<br>Asp        | tgg<br>Trp<br>360 | aca<br>Thr        | gaa<br>Glu        | aat<br>Asn        | ctc<br>Leu        | ata<br>Ile<br>365 | agg<br>Arg        | 1225 |
| aca<br>Thr        | ttt<br>Phe        | gaa<br>Glu        | caa<br>Gln<br>370 | cag<br>Gln        | cac<br>His        | tca<br>Ser        | cca<br>Pro        | atg<br>Met<br>375 | ccc<br>Pro        | agg<br>Arg        | atc<br>Ile        | gag<br>Glu        | gtg<br>Val<br>380 | gat<br>Asp        | ggt<br>Gly        | 1273 |
| ccc<br>Pro        | ttt<br>Phe        | ggc<br>Gly<br>385 | aca<br>Thr        | gtc<br>Val        | agt<br>Ser        | gag<br>Glu        | gat<br>Asp<br>390 | gtc<br>Val        | ttc<br>Phe        | cag<br>Gln        | tac<br>Tyr        | gaa<br>Glu<br>395 | gtg<br>Val        | gct<br>Ala        | gta<br>Val        | 1321 |
| ctg<br>Leu        | gtt<br>Val<br>400 | ggg<br>Gly        | gca<br>Ala        | ggg<br>Gly        | att<br>Ile        | ggc<br>Gly<br>405 | gtc<br>Val        | act<br>Thr        | ccc<br>Pro        | ttt<br>Phe        | gct<br>Ala<br>410 | tcc<br>Ser        | ttc<br>Phe        | ttg<br>Leu        | aaa<br>Lys        | 1369 |
| tct<br>Ser<br>415 | atc<br>Ile        | tgg<br>Trp        | tac<br>Tyr        | aaa<br>Lys        | ttc<br>Phe<br>420 | cag<br>Gln        | cgt<br>Arg        | gca<br>Ala        | cac<br>His        | aac<br>Asn<br>425 | aag<br>Lys        | ctg<br>Leu        | aaa<br>Lys        | aca<br>Thr        | caa<br>G1n<br>430 | 1417 |
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| ttc aac aac tta ttg aat tcc ctg gaa caa gag atg gac gaa tta ggc<br>Phe Asn Asn Leu Leu Asn Ser Leu Glu Gln Glu Met Asp Glu Leu Gly<br>450 455 460     | 1513 |
|---|------|
| aaa ccg gat ttc cta aac tac cga ctc ttc ctc act ggc tgg gat agc<br>Lys Pro Asp Phe Leu Asn Tyr Arg Leu Phe Leu Thr Gly Trp Asp Ser<br>465 470 475     | 1561 |
| aac att gct ggt cat gca gca tta aac ttt gac aga gcc act gac gtc<br>Asn Ile Ala Gly His Ala Ala Leu Asn Phe Asp Arg Ala Thr Asp Val<br>480 485 490     | 1609 |
| ctg aca ggt ctg aaa cag aaa acc tcc ttt ggg aga cca atg tgg gac<br>Leu Thr Gly Leu Lys Gln Lys Thr Ser Phe Gly Arg Pro Met Trp Asp<br>495 500 505 510 | 1657 |
| aat gag ttt tct aga ata gct act gcc cac ccc aag tct gtg gtg ggg<br>Asn Glu Phe Ser Arg Ile Ala Thr Ala His Pro Lys Ser Val Val Gly<br>515 520 525     | 1705 |
| gtt ttc tta tgc ggc cct ccg act ttg gca aaa agc ctg cgc aaa tgc<br>Val Phe Leu Cys Gly Pro Pro Thr Leu Ala Lys Ser Leu Arg Lys Cys<br>530 535 540     | 1753 |
| tgt cgg cgg tac tca agt ctg gat cct agg aag gtt caa ttc tac ttc<br>Cys Arg Arg Tyr Ser Ser Leu Asp Pro Arg Lys Val Gln Phe Tyr Phe<br>545 550 555     | 1801 |
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Ala Leu Ala Leu Ala Arg Ala Ser Ala Leu Cys Leu Asn Phe Asn Ser 50 60

Met Val Ile Leu Ile Pro Val Cys Arg Asn Leu Leu Ser Phe Leu Arg 65 70 75 80

Gly Thr Cys Ser Phe Cys Asn His Thr Leu Arg Lys Pro Leu Asp His 85 90 95

Asn Leu Thr Phe His Lys Leu Val Ala Tyr Met Ile Cys Ile Phe Thr 100 105 110

Ala Ile His Ile Ile Ala His Leu Phe Asn Phe Glu Arg Tyr Ser Arg 115 120 125

Ser Gln Gln Ala Met Asp Gly Ser Leu Ala Ser Val Leu Ser Ser Leu 130 140

Phe His Pro Glu Lys Glu Asp Ser Trp Leu Asn Pro Ile Gln Ser Pro 145 150 155 160

Asn Val Thr Val Met Tyr Ala Ala Phe Thr Ser Ile Ala Gly Leu Thr 165 170 175

Gly Val Val Ala Thr Val Ala Leu Val Leu Met Val Thr Ser Ala Met 180 185 190

Glu Phe Ile Arg Arg Asn Tyr Phe Glu Leu Phe Trp Tyr Thr His His 195 200 205

Leu Phe Ile Ile Tyr Ile Ile Cys Leu Gly Ile His Gly Leu Gly Gly 210 215 220

Ile Val Arg Gly Gln Thr Glu Glu Ser Met Ser Glu Ser His Pro Arg 225 230 235 240

Asn Cys Ser Tyr Ser Phe His Glu Trp Asp Lys Tyr Glu Arg Ser Cys 255 Page 9

Arg Ser Pro His Phe Val Gly Gln Pro Pro Glu Ser Trp Lys Trp Ile 260 265 270 Leu Ala Pro Ile Ala Phe Tyr Ile Phe Glu Arg Ile Leu Arg Phe Tyr 275 280 285 Arg Ser Arg Gln Lys Val Val Ile Thr Lys Val Val Met His Pro Cys 290 295 300 Lys Val Leu Glu Leu Gln Met Arg Lys Arg Gly Phe Thr Met Gly Ile 305 310 315 320Gly Gln Tyr Ile Phe Val Asn Cys Pro Ser Ile Ser Phe Leu Glu Trp 325 330 335 His Pro Phe Thr Leu Thr Ser Ala Pro Glu Glu Glu Phe Phe Ser Ile 340 345 350His Ile Arg Ala Ala Gly Asp Trp Thr Glu Asn Leu Ile Arg Thr Phe 355 360 365 Glu Gln Gln His Ser Pro Met Pro Arg Ile Glu Val Asp Gly Pro Phe 370 380 Gly Thr Val Ser Glu Asp Val Phe Gln Tyr Glu Val Ala Val Leu Val 385 390 395 400 Gly Ala Gly Ile Gly Val Thr Pro Phe Ala Ser Phe Leu Lys Ser Ile  $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$ Trp Tyr Lys Phe Gln Arg Ala His Asn Lys Leu Lys Thr Gln Lys Ile 420 425 430 Tyr Phe Tyr Trp Ile Cys Arg Glu Thr Gly Ala Phe Ala Trp Phe Asn 435 440 445 Asn Leu Leu Asn Ser Leu Glu Gln Glu Met Asp Glu Leu Gly Lys Pro 450 460 Asp Phe Leu Asn Tyr Arg Leu Phe Leu Thr Gly Trp Asp Ser Asn Ile 465 470 475 480 Ala Gly His Ala Ala Leu Asn Phe Asp Arg Ala Thr Asp Val Leu Thr 485 490 495 Gly Leu Lys Gln Lys Thr Ser Phe Gly Arg Pro Met Trp Asp Asn Glu 500 510 Phe Ser Arg Ile Ala Thr Ala His Pro Lys Ser Val Val Gly Val Phe Leu Cys Gly Pro Pro Thr Leu Ala Lys Ser Leu Arg Lys Cys Cys Arg 530 540

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